

CLAIMS

What is claimed as the invention is:

1. A method for producing differentiated cells from a donor culture of undifferentiated primate pluripotent stem (pPS) cells, comprising:
  - a) preparing a suspension of pPS cells from the undifferentiated donor culture;
  - b) replating and culturing the suspended cells on a solid surface so that they differentiate without forming embryoid bodies; and
  - c) harvesting differentiated cells from the solid surface.
2. A method for obtaining differentiated cells from a donor culture of undifferentiated primate pluripotent stem (pPS) cells, comprising:
  - a) culturing the pPS cells on a solid surface in an environment essentially free of feeder cells;
  - b) changing medium used to culture the cells so that they differentiate before there is overgrowth or formation of colonies; and
  - c) harvesting differentiated cells from the solid surface.
3. The method of claim 1, wherein the donor culture comprises both undifferentiated pPS cells and feeder cells, which are replated onto a solid surface without adding fresh feeder cells.
4. The method of claim 1, wherein the donor culture is essentially free of feeder cells, which are replated on a solid surface without any extracellular matrix.
5. The method of claim 1, wherein the solid surface bears a polycation.
6. The method of claim 5, wherein the polycation is polyornithine.
7. The method of claim 1, wherein the cells are cultured after replating in a medium containing a factor that promotes differentiation.
8. The method of claim 7, wherein the factor is Brain Derived Neurotrophic Factor (BDNF) or Neutrotrophin-3 (NT-3).
9. The method of claim 2, wherein the changed medium is essentially free of fibroblast growth factor.
10. The method of claim 2, wherein the changed medium contains Brain Derived Neurotrophic Factor (BDNF) or Neutrotrophin-3 (NT-3).
11. The method of claim 2, wherein the changed medium contains noggin or follistatin.

12. The method of claim 1, whereby cells cultured on the solid surface differentiate to precursor cells committed to a restricted cell lineage and capable of proliferation.
13. The method of claim 12, wherein the precursor cells are ectodermal cells.
14. The method of claim 13, wherein the precursor cells are committed to the neuroectoderm lineage.
15. The method of claim 14, wherein the precursor cells are cells of the mesoderm, endoderm or visceral endoderm.
16. The method of claim 1, whereby cells cultured on the solid surface become fully differentiated cells.
17. The method of claim 16, wherein the fully differentiated cells are neurons or glial cells.
18. The method of claim 17, wherein at least ~10% of the cells staining positive for MAP-2 are also positive for tyrosine hydroxylase.
19. Committed precursor cells prepared according to the method of claim 12.
20. Fully differentiated cells prepared according to the method of claim 16.
21. A method of screening a compound for cellular toxicity or modulation, comprising combining the compound with a committed or differentiated cell prepared according to the method of claim 1, determining any phenotypic or metabolic changes in the cell that result from contact with the compound, and correlating the change with cellular toxicity or modulation.
22. A method for obtaining a polynucleotide comprising a nucleotide sequence contained in an mRNA that is expressed at a different level in committed or differentiated cells prepared according to the method of claim 1, compared with undifferentiated primate pluripotent stem (pPS) cells, the method comprising:
  - a) determining the level of expression of a plurality of mRNAs in committed or differentiated cells, in comparison to the level of expression of the same mRNAs in undifferentiated pPS cells;
  - b) identifying an mRNA expressed at a different level in the committed or differentiated cells, relative to the undifferentiated pPS cells; and
  - c) preparing a polynucleotide comprising a nucleotide sequence of at least 30 consecutive nucleotides contained in the identified mRNA.